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EDITORIAL COMMENT

Viability, Prognosis, Revascularization, and Pascal*

David S. Bach, MD, FACC
Ann Arbor, Michigan

The presence and severity of ischemic left ventricular (LV) systolic dysfunction is an important predictor of prognosis. There are ample data demonstrating that for patients with coronary artery disease and ischemic LV dysfunction, revascularization is associated with a better prognosis compared with medical therapy alone. In addition, varying degrees of recovery of LV dysfunction can be observed after revascularization. To predict which patients will benefit most from surgical revascularization (and possibly which patients may not benefit at all), attempts have been made to prospectively assess the extent of myocardium that is dysfunctional but viable. However, the published literature on testing for myocardial viability is complicated, with conclusions that are sometimes contradictory. To a large degree, this is due to the disparate clinical scenarios in which myocardial viability is evaluated, the different noninvasive techniques used for its assessment, the vagaries of revascularization, and the variety of outcomes measured.

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What is viable myocardium? The word "viable" implies that something is living or cable of germination. However, the term has been employed with varying meanings in the context of ischemic heart disease. Myocardium that is normally perfused and has normal contractile function is obviously alive. Myocardial viability is typically questioned in the setting of ischemic dysfunction, which occurs in two settings: "stunning" is transient myocardial dysfunction that complicates an acute cardiac event, whereas "hibernation" is mechanical dysfunction that occurs because of ongoing severe, chronic ischemia (1). Although it is probably easier to detect than hibernating myocardium, stunned myocardium recovers with the passage of time, and its identification is therefore of relatively less importance. In contrast, hibernating myocardium will not recover function without relief of ischemia, typically with revascularization. Its detection relies on the demonstration of intact metabolism on positron emission tomography, preserved cell membrane integrity as a measure of cellular perfusion using nuclear scintigraphy (and perhaps someday with myocardial contrast echocardiography), or contractile reserve using inotropic stimulation and echocardiographic or magnetic resonance imaging.

Because hibernating myocardium is subtended by a critically stenosed coronary artery, tracer uptake may be abnormal, and demonstration of contractile reserve may be limited by a competing ischemic response. Demonstration of viability is further confounded by the heterogeneous nature of dysfunctional myocardium, often involving partial-thickness infarction in the same location (2).

Several "gold standards" have been used against which testing for viable myocardium is judged. Recovery of regional or global mechanical function after revascularization serves as an attractive end point. However, recovery of function is affected by other variables, including the extent of partial-thickness infarction, the adequacy of revascularization, intervening ischemic events between revascularization and follow-up imaging, and concomitant medical therapy. For these reasons, "viable" myocardium should never have been taken as synonymous with "capable of recovering mechanical function." The strongest observations to support this view relate to the prognostic implications of revascularization independent of mechanical recovery.

Prognostic importance of viability. The existence of viable myocardium among patients with ischemic LV dysfunction is a blade that cuts both ways. Among patients who undergo revascularization, the presence of viable myocardium portends the potential for symptomatic improvement (3–5), recovery of mechanical function (5), and superior prognosis (5,6). However, among patients who do not undergo revascularization, viable myocardium is a marker for poor prognosis (7,8). It appears that viable myocardium is a boon if the patient undergoes revascularization and a bane if the patient does not.

In an earlier editorial in the *Journal* (9) that accompanied another study addressing myocardial viability testing and prognosis, the question was raised whether it could be justified to simply consider revascularization in all patients with coronary artery disease and ischemic LV dysfunction. However, the idea was doomed with perhaps the worst that medical literature has available: noting that supporting data are from nonrandomized studies in the surgical literature. However, the issue remains pertinent. Knowledge that patients with viable myocardium fare better after revascularization than do those without viable myocardium is not an argument to deny revascularization to patients without viable myocardium. With the vagaries of myocardial viability testing, what is the appropriate level of certainty that viable myocardium is absent?

In this issue of the *Journal*, Sawada et al. (10) address the incremental value of myocardial viability detected using low-dose dobutamine stress echocardiography on the prediction of prognosis five years after surgical revascularization. They found that prognosis after coronary bypass surgery is related to the presence and extent of viable myocardium, and that the data contributed by low-dose

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From the Department of Medicine, Division of Cardiology, University of Michigan, Ann Arbor, Michigan.

dobutamine stress echocardiography are complementary to clinical information and data derived from the baseline echocardiogram. Several criteria were used to test the presence of viability, including several measures of contractile reserve. Interestingly, measures of contractile reserve were not predictive of prognosis after coronary bypass grafting, whereas the simpler measure of wall motion score index at low stress was.

How should viability be measured on echo? The failure of contractile reserve to discriminate outcomes may come as no surprise to those who read echocardiograms and attempt to discern subtle changes in contractility in severely dysfunctional myocardium. The interaction between severe underlying coronary stenosis, hibernation, intermittent stunning, previous partial-thickness infarction, and a competing ischemic response makes the reliable identification of contractile reserve a challenge at best. Although a "biphasic response" on dobutamine stress echocardiograph is a specific predictor of mechanical recovery after revascularization (11), it is insensitive compared with simpler measures such as wall thickness (12).

Wall motion score index is far from a precise measure of LV function. The ventricle is nominally divided into 16 segments that bear some relationship to coronary anatomy, and a semiquantitative system is used to classify contractility, dividing the sum of the scores of individual segments by the number of segments scored. However, assigning numerical values to qualitative descriptors is problematic. Is a segment scored as "4" (dyskinetic) twice as bad as one scored as "2" (hypokinetic)? Are the implications the same if all of the left ventricle is hypokinetic as if half is normal and half is akinetic, both with a wall motion score index of 2.0?

Ultimately, the shortfalls of the wall motion score index may also be its advantage, and its use underscores the value of the present study (10). Whereas other more esoteric measures of myocardial viability may have appeal, calculating low-dose dobutamine wall motion score index is feasible and reproducible. It incorporates data reflecting regional and global contractile function as well as the presence of ventricular aneurysm.

Limitations of the data. The study as presented assumes that revascularization was complete if all diseased vessels were bypassed. The quality of the diseased vessel and the possibility of subsequent occlusion were not tested. As Sawada et al. (10) note, the study was conducted over a time of active evolution in medical therapy for ischemic LV dysfunction, raising the question of whether the results would be the same if the study were repeated using present "state-of-the-art" medical therapy. There was the paradoxical finding that therapy with an angiotensin-converting enzyme inhibitor was associated with worse outcome, presumably owing to its relationship to severity of congestive heart failure rather than as an independent effect. The study is based on surgical revascularization, and it is not known whether the findings can be extrapolated to percutaneous intervention.

Identifying candidates for coronary artery bypass surgery. The study by Sawada et al. (10) addresses the survival advantage associated with the presence and extent of viable myocardium among patients with severe LV systolic dysfunction undergoing surgical coronary revascularization. It does not address whether surgical revascularization has advantages compared with medical therapy. Earlier studies have demonstrated that patients with LV dysfunction and viable myocardium fare better with revascularization than with medical therapy alone (6–8,11). However, what of patients without demonstrable myocardial viability?

A meta-analysis published in 2002 found that among patients with ischemic LV dysfunction but without myocardial viability, there was no significant difference in survival between surgical intervention and medical therapy (6). Earlier this year, Meluzín et al. (13) demonstrated a trend that did not reach statistical significance toward better survival with surgery (67% vs. 50% at 5 years) in the absence of myocardial viability. From the surgical literature, Di Carli et al. (14) demonstrated a trend toward better survival with surgery in the absence of viable myocardium on positron emission tomography if there were symptoms of angina (100% vs. 60% at 4 years, $p = 0.085$). Finally, Kleinkamp et al. (15) reported that although the presence of viability was associated with survival benefit with surgical revascularization, the quality of the coronary arteries was a stronger predictor of benefit. Although none of these studies proves a survival advantage with surgery in patients without demonstrable viability, some reveal a trend favoring revascularization and none show a detrimental effect. It is unknown whether the absence of a statistically significant improvement in survival with surgery is due to no actual survival advantage; a smaller advantage than among patients with viable myocardium, such that trends fail to reach statistical significance; or heterogeneity of the population without demonstrable myocardium, such that some patients benefit and others do not.

Pascal's Wager and coronary revascularization. The seventeenth-century mathematician Blaise Pascal is perhaps best known for Pascal's triangle, a mathematical array in which each entry is the sum of the two numbers directly above it. A philosopher, Pascal is also known for Pascal's Wager: "If you believe in God and turn out to be incorrect, you have lost nothing—but if you don't believe in God and turn out to be incorrect, you will go to hell. Therefore it is foolish to be an atheist." Religious implications notwithstanding, the message is that decisions should weigh consequences in addition to probabilities.

Prognosis is poor among patients with coronary artery disease and severe LV dysfunction, and improved with surgical revascularization. The presence of viable myocardium is a strong predictor of improved survival with revascularization, but a marker for worse prognosis without revascularization. For patients with viable myocardium, there appears to be no remaining uncertainty that revascularization is indicated; future research will continue to define

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the respective roles of surgical and percutaneous techniques even as both continue to evolve. However, the detection of viability is not exact, and available tests are imperfect. Because coronary artery bypass surgery does not appear to adversely affect survival in the absence of viable myocardium, why not exclude patients who are at especially high risk for bypass surgery (16) and refer the rest for revascularization?

Because it is appropriate to weigh consequences in addition to probabilities, the risks of failing to intervene should be considered, realizing that testing for viability is imperfect. Among patients with severe LV systolic dysfunction and reasonable surgical targets who are not at excessive risk for surgical revascularization, the consequences of failing to intervene may outweigh the risks of intervention, even if testing fails to detect viable myocardium. Specifically, in the absence of a contraindication, it may be very reasonable to intervene regardless of the presence or absence of viability.

Should we test for viability at all? If patients undergo revascularization regardless of the results, there is little rationale for preoperative testing. Some patients will still fall into "gray" areas, with moderate or greater risk for surgery and arterial targets that are less than ideal. Among such patients, testing for myocardial viability provides useful data that could help sway decisions toward or away from intervention. However, among patients in whom risk is not excessive, it may be the most prudent option to perform revascularization without testing for viability. Although some patients benefit from intervention more than others do, the risks of not intervening mitigate against a more conservative strategy.

Reprint requests and correspondence: Dr. David S. Bach, University of Michigan, L3119 Women's-0273, 1500 Medical Center Drive, Ann Arbor, Michigan 48109. E-mail: dbach@umich.edu.

REFERENCES

1. Bolli R. Myocardial 'stunning' in man. Circulation 1992;86:1671–91.
2. Armstrong WF. "Hibernating" myocardium: asleep or part dead. J Am Coll Cardiol 1996;28:530–5.
3. Di Carli MF, Asgarzadie F, Schelbert HR, et al. Quantitative relation between myocardial viability and improvement in heart failure symptoms after revascularization in patients with ischemic cardiomyopathy. Circulation 1995;92:3436–44.
4. Marwick TH, Zuchowski C, Lauer MS, Secknus MA, Williams MJ, Lytle BW. Functional status and quality of life in patients with heart failure undergoing coronary artery bypass surgery after assessment of myocardial viability. J Am Coll Cardiol 1999;33:750–8.
5. Bax JJ, Poldermans D, Elhendy A, et al. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. J Am Coll Cardiol 1999;34:163–9.
6. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. J Am Coll Cardiol 2002;39:1151–8.
7. Williams MJ, Odabashian J, Lauer MS, Thomas JD, Marwick TH. Prognostic value of dobutamine echocardiography in patients with left ventricular dysfunction. J Am Coll Cardiol 1996;27:132–9.
8. Beanlands RSB, Hendry PJ, Masters RG, deKemp RA, Woodend K, Ruddy TD. Delay in revascularization is associated with increased mortality rate in patients with severe left ventricular dysfunction and viable myocardium on fluorine 18-fluordeoxyglucose positron emission tomography imaging. Circulation 1998;98:II51–6.
9. Bonow RO. Myocardial viability and prognosis in patients with ischemic left ventricular dysfunction. J Am Coll Cardiol 2002;39:1159–62.
10. Sawada S, Bapat A, Vaz D, et al. Incremental value of myocardial viability for prediction of long-term prognosis in surgically revascularized patients with left ventricular dysfunction. J Am Coll Cardiol 2003;42:2099–105.
11. Afridi I, Grayburn PA, Panza JA, Oh JK, Zoghbi WA, Marwick TH. Myocardial viability during dobutamine echocardiography predicts survival in patients with coronary artery disease and severe left ventricular systolic dysfunction. J Am Coll Cardiol 1998;32:921–6.
12. Cwajg JM, Cwajg E, Nagueh SF, et al. End-diastolic wall thickness as a predictor of recovery of function in myocardial hibernation. J Am Coll Cardiol 2000;35:1152–61.
13. Mezulín J, Cerny, Spinarova L, et al. Prognosis in patients with chronic coronary artery disease and severe left ventricular dysfunction: the importance of myocardial viability. Eur J Heart Fail 2003;5:85–93.
14. Di Carli MF, Maddahi J, Rokhsar S, et al. Long-term survival of patients with chronic coronary artery disease and left ventricular dysfunction: implications for the role of myocardial viability assessment in management decisions. J Thorac Cardiovasc Surg 1998;116:997–1004.
15. Kleinkamp G, Maleszka A, Reiss N, Stüttgen B, Körfer R. Determinants of mid- and long-term results in patients after surgical revascularization for ischemic cardiomyopathy. Ann Thorac Surg 2003;75:1406–13.
16. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA guidelines for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). J Am Coll Cardiol 1999;34:1262–346.